

C¹ 3 sequence encoding the enzyme subunit or fragment is not operably linked to a transcription control
4 element, and wherein said subunit or fragment is active when combined with a further subunit.

1 12. (Amended) The combination of:
2 SUB E3 (i) a DNA construct for integration into the genome of an eukaryotic cell
3 comprising a sequence encoding a first indicator component under the control of a promoter having
4 restricted expression; and
5 (ii) a DNA construct for integration into the genome of a eukaryotic cell,
C² 6 comprising in the 5' to 3' direction, a splice acceptor, a sequence encoding a second indicator
7 component not operably linked to a transcription control element, and an optional IRES, wherein
8 expression of both the first and second indicator components in said cell is detectable.

SUB D3 1 13. (Amended) A eukaryotic cell transformed by the combination of DNA
2 constructs of claim 12.

1 14. (Amended) A DNA construct comprising, in a 5' to 3' direction, a splice acceptor
2 and a sequence encoding an inactive alpha or omega fragment of β -galactosidase, wherein said
C³ 3 sequence encoding the inactive alpha or omega fragment is not operably linked to a transcription
4 control element and said fragment is active when combined with another fragment of β -
5 galactosidase.

1 19. (Amended) A method of producing a mouse comprising a detectable indicator
2 associated with a target gene having restricted expression, which comprises:
3 (i) transforming a murine ES cell by integrating into the cell's genome, a first
4 DNA construct encoding a first indicator component under the control of a promoter having
5 restricted expression;
6 (ii) transforming the cell of (i) or a descendent of the cell by integrating into the
7 cell's genome, a second DNA construct comprising DNA encoding a second indicator component
8 not operably linked to a transcription control element;
9 (iii) selecting transformed cells of (ii);
10 (iv) introducing selected cells of (iii) into a murine or porcine host embryo;
11 (v) implanting the host embryo of (iv) into a pseudopregnant mammal;

12 *sub* (vi) maintaining the mammal of (v) while offspring develops to term from the host
13 *file* embryo; and

14 (vii) selecting offspring of (vi) by the presence of a detectable indicator resulting
15 from both the first and second indicator components in tissue or specialized cells of the offspring.
